REPORT OF COUNCIL ON SCIENTIFIC AFFAIRS

CSA Report 1-I-02

Subject: Black Mold and Human Illness

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Over the past several years, increasing public attention has focused on a potential or suspected role in human illness from the mold *Stachybotrys chartarum*, commonly known as "black mold," particularly in association with water-damaged buildings. In Texas, this attention has been manifest not in scientific or medical publications, but rather in the lay press and in an increasing number of insurance claims filed for mold remediation of homes and workplaces. Texas Medical Association's Council on Scientific Affairs has been asked to update the "state of the medical science" in this important area.

To study this issue, the council conducted a search of medical and scientific literature and contacted Texas and national experts/specialists. After reviewing available data, the council has concluded that public concern for adverse health effects from inhalation of *Stachybotrys* spores in water-damaged buildings is generally not supported by published reports in medical literature.

Recommendation: Approval of the attached policy paper on black mold and human illness.

Related 2002-03 Strategic Priority: Expend political capital to promote and strengthen Texas' public health infrastructure.

HOUSE ACTION: Approved conclusions and recommendations as policy; filed remainder of report.

BLACK MOLD AND HUMAN ILLNESS
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INTERACTIONS OF HUMANS WITH AGENTS IN THEIR ENVIRONMENT

Living organisms capable of causing infection or other types of illnesses are everywhere in our environment. In addition to molds and other fungi, these include bacteria, viruses, protozoa, and helminthes. Infections are by far the most common forms of human illness produced by exposure to these organisms. These are generally combated or prevented by our natural host defenses, which include protein antibodies and cell-mediated immunity. In recent times, anti-microbial drugs have substantially augmented these natural defenses against environmental agents.

The human immune and inflammatory systems protect us from a multitude of these and other agents in our environment, usually by one or more of the following four general types of immune reactions: [1]

1. Type I reactions are mediated by IgE antibodies and are the cause of most "allergic" reactions. Approximately 8 to10 percent of the population have adverse symptoms due to Type I reactions to pollens, dust, mold, animal dander, or food.
2. Type II (cytotoxic) reactions target molecules on the surface of cells and initiate processes leading to the death of that specific cell (hemolytic anemia).
3. Type III reactions are "immune-complex" reactions in which a protective antibody attaches to an antigen and initiates an inflammatory reaction (glomerulonephritis).
4. Type IV reactions (cell-mediated immunity) is important in immunity to foreign tissues (organ transplantation), certain infectious agents (tuberculosis), chemicals (contact dermatitis), and in cancer biology.

Once specificity is provided by the immune system, effector systems are responsible for neutralization or eradication of the environmental agent. This is accomplished by inflammatory cells, cytokines, and other chemical mediators.

Still, a minority of persons develop an illness or other adverse manifestation from contact with environmental agents. These adverse effects might take the form of allergies or other immune reactions, or autoimmunity. Autoimmunity, for which there are clear genetic and other factors, is generally thought to be caused by failure of the immune system to recognize parts of the body as "self."

POTENTIAL HEALTH ISSUES RELATED TO MOLD EXPOSURE

In theory, there are five ways in which molds could produce or aggravate human illness or otherwise contribute to symptoms:

1. Type I immune reactions, which can lead to allergic rhinitis (nasal discharge, sneezing, conjunctivitis) or asthma (bronchospasm, wheezing, mucous secretion and plugging).
2. Irritation to mucous membranes through mold production of volatile organic compounds (VOCs) in a manner analogous to non-mold irritants, e.g., tobacco smoke, gas/kerosene stove emissions, ozone.
3. Type III immune reaction, examples including hypersensitivity pneumonitis, which includes "farmer's lung" (lung tissue inflammation occurring from exposure of an inhaled antigen), and allergic aspergillosis (a rare lung tissue inflammation involving both airways and tissues in the lungs).[3]

4. Toxic reaction from mold products (mycotoxins).
5. Toxic reaction from microbial byproducts (endotoxins).[4]

Infectious health issues related to mold exposure can occur in both normal and immuno-compromised individuals. Normal persons may experience the overgrowth of candida normally found in vaginal and oral cavities after treatment with antimicrobial drugs that alter the dominant normal microbial flora. Another example is chronic dermatophyte infection of skin (athlete's foot) or nails. Immunocompromised individuals often have true infections with tissue damage when microbes that may be present in the body or environment overgrow and invade body tissues. Examples include re-activation of tuberculosis, histoplasmosis, coccidiomycosis, and invasive candidiasis.

The prior reported occasional syndromes associated with residential fungal exposure primarily have been hypersensitivity pneumonitis.[5-10] Human colonization by other environmental fungi also has been reported to cause chronic allergic sinusitis.[11] The cases of hypersensitivity pneumonia reports are case reports; only one has described *Stachybotrys* as the causal agent.[5]

Ingestion of mycotoxins in foods has been of concern for some time, and there are widespread efforts to protect our food supplies from such agents. Inhalation exposure outside of agricultural or industrial settings has been thought to be insufficient to produce much morbidity.[12]

Several molds commonly found in homes, including *Stachybotrys,* are capable of producing mycotoxins. In vitro (laboratory only), some mycotoxins are capable of blunting the phagocytic removal of particulate matter. Our knowledge about mycotoxins is very incomplete regarding dose-health effects relationships, how to measure them in environmental samples, or to detect them in patient samples.[12]

STACHYBOTRYS LITERATURE SUMMARY

A summary of available literature on *Stachybotrys* reveals that it is commonly found in water-damaged buildings and dwellings, as are many other molds. However, there is no convincing evidence that *Stachybotrys* is a significant or even proven pathogenic antigen in either traditional allergic reactions (Type I hypersensitivity) or the rare forms of hypersensitivity pneumonitis (Type III hypersensitivity). The only report in the peer-reviewed medical literature suggesting a potentially significant causative role for *Stachybotrys* in human illness is a report of pulmonary hemorrhage in infants thought to be (but not proven to be) caused by *Stachybotrys* mycotoxin. Re-examination of this presumed outbreak has identified shortcomings in the implementation and reporting of the investigation. These reviews have "led CDC to conclude that a possible association between acute pulmonary hemorrhage/hemosiderosis in infants and exposure to molds, specifically *Stachybotrys chartarum*, commonly referred to by its synonym *Stachybotrys atra*, was not proven."[13] The original report was based on suggestive epidemiological evidence rather than proof.[14]

The "state of the science" is perhaps best expressed by Dearborn in his paper "Health Effects of Molds and Mycotoxins" at the 55th Annual Meeting of the American Academy of Allergy and Immunology, March 2002.[12]

> There are major limitations to our better understanding of the potential health impact of chronic toxigenic mold exposure. The exposures are to multiple fungi with varied amounts and types of mycotoxins. Most of the symptoms are rather subjective and difficult to objectively measure. While quantitative identification of fungi in indoor environments is improving, quantification of

even some of the mycotoxins is at best expensive. Epidemiologic studies are greatly hampered by the lack of either acute or chronic biomarkers of exposure. Controversy, overreaction, and inadequate public health prudence will continue until these challenges are adequately addressed.

Terr expressed a similar opinion in a review that examined and critiqued the published literature on *Stachybotrys*. This review found *Stachybotrys* to be a minor component of the indoor mycoflora, found on certain building material surfaces in water-damaged buildings. However, airborne spores are present in such low concentrations that they are unlikely to cause illness. [15]

Page and Trout reported in 1998 on a MEDLINE search strategy that located 13 articles on fungi, mycotoxins, and the indoor environment. They concluded that the literature contained inadequate evidence to support a causal relationship between symptoms or illness among building occupants and exposure to mycotoxins. They recommended, "that research involving the identification and isolation of specific fungal toxins in the environment and in humans is needed before a more definitive link between health outcomes and mycotoxins can be made."[16]

In summary, the hypothesis that exposure to molds and their toxic products may lead to adverse health effects can be made. However, the proposition that molds in indoor environments may lead to adverse health effects through mechanisms other than infection and allergic/immunologic reactions is an untested impression.

EVIDENCE REQUIRED TO VALIDATE AN ENVIRONMENTAL AGENT AS CONTRIBUTORY TO HUMAN ILLNESS

Koch's postulates are one method to test the concept that molds in the indoor environment may be health hazards. Formulated in 1882, the postulates remain the standard of proof for infectious or toxic agents and would be the logical and favored form of proof of causation of human illness by *Stachybotrys*.

In short, these postulates hold that:

- A pathogenic organism or agent should be associated significantly more often with the illness or syndrome than similar but non-pathogenic organisms;
- A pathogenic organism or agent should produce the same or substantially similar pathology in appropriate animal models;
- The animal model host must become consistently affected using a natural route (even exposure to a known human pathogen does not uniformly lead to disease in all humans); and
- The return of the suspected causative agent to a human host should produce consistently the features of the illness or syndrome.[2]

Scientific and medical knowledge is built using both direct and indirect evidence. Evidence is indirect if two or more bodies of evidence are required to relate the exposure or intervention of interest to the principal health outcome. More recent methodology has augmented the strength of associations and statistical inferences regarding disease etiology, diagnosis, therapy or interventions, prognosis, and outcomes.[3] These evidence categories, in decreasing order of validity, include:

- Primary studies in humans, particularly large, randomized controlled trials as well as meta-analyses of randomized controlled trials, are recognized as best (small trials are less valid). Nonrandomized

controlled trials, cohort or longitudinal studies, case-control studies, case series, and reports are less robust, especially the latter two;

- Non-human studies (laboratory studies, animal studies); and
- Syntheses (systematic reviews).

EVALUATING THE ROLE OF STACHYBOTRYS IN "SICK BUILDING SYNDROME"

Bernstein has suggested an approach to suspected building-related illness that includes:[17]

(1) a thorough history (duration and nature of symptoms, home environmental and workplace history, past medical history, family history);
(2) a physical exam;
(3) exclusion of more common infectious causes;
(4) phenotyping the patient as atopic versus non-atopic (skin testing to seasonal and perennial allergens including a mold panel [or corresponding serologic testing], spirometry pre-/post-bronchodilator);
(5) chest x-ray or high-resolution CT of chest (to determine if pulmonary findings consistent with hypersensitivity pneumonitis are present and require additional evaluation);
(6) supportive testing including serologic testing for specific IgG, IgE, or IgA to mold (including *Stachybotrys*), hypersensitivity pneumonitis screen (precipitating antibodies), and consideration of humoral and cell-mediated immune system evaluation;
(7) environmental assessment including walkthrough, air sampling, and measurement of known perennial allergens, irritants (VOCs and chemicals [nitrous dioxide, sulfur dioxide, ozone]), dew point, and mycotoxins;
(8) measurement of total symptom scores in and out of the environment;
(9) measurement of peak expiratory flow rates in and out of the environment event every 2-3 hours while awake and correlation with environmental exposure measurements; and
(10) consideration of specific provocation test (nasal challenge preferred to the more risky bronchoprovocation).

Evidence-based effective interventions for reducing specific types of allergen loads include bedding encasements (dust mites, cat dander, mold), HEPA filtration (cat and dog dander), HEPA vacuum (cat and dog dander, dust mites, cockroach), dehumidification (<50 percent) with air conditioning or dehumidifiers (dust mites, mold, cockroach), and thorough cleaning (cockroach).[18]

Other common but less proven methods for reducing allergen loads include air conditioning or other measure to filter outdoor air, removal of carpets, hot (>130° F) washing of bedding, repair of leaky basements, and changes in home and building design. Patient compliance with these measures usually runs 35 percent or less.[18]

CSA CONCLUSIONS

Adverse health effects from inhalation of *Stachybotrys* spores in water-damaged buildings is not supported by available peer-reviewed reports in medical literature.

The probability or possibility of causation or exacerbation of a medical condition due to exposure to mold in indoor environments currently exists only for the following:

- Traditional Type I immune reactions (allergies, with correlation of symptoms with exposure and in vitro demonstration of IgE antibodies by allergy skin tests or RAST test for specific IgE antibodies in blood samples); and
- Rare Type III immune reactions (hypersensitivity pneumonitis), pulmonary hemorrhage in infants associated with mycotoxins.

Further, for *Stachybotrys* or other molds to be implicated in other disease models, the following must be present:

- Peer-reviewed medical literature should show clearly that such mold or mold by-product has produced clinical manifestations similar to those displayed by the patient;
- Evidence of personal causation of the type described by references 17 and 18 must exist.

RECOMMENDATIONS

The Council on Scientific Affairs recommends that TMA:

(1) support the need for continued scientific research regarding the impact of molds on human health, especially the effects of mycotoxins;
(2) educate our membership regarding this issue, including the use of Koch's Postulates as the means to validate illness caused by *Stachybotrys*, through information in TMA publications and on the TMA web site;
(3) communicate the information in this paper to the appropriate state governmental agencies, such as the Texas Attorney General, Texas Department of Health, Texas Department of Insurance, and others;
(4) support that remediation of water damage in homes and other buildings should generally be based on non-clinical factors, unless clear medical evidence, as described in this paper, exists to demonstrate the role of *Stachybotrys* in a particular case of illness; and
(5) provide educational information on this topic on the TMA web site for interested clinical personnel as well as the general public.

OTHER PHYSICIAN REVIEWERS

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William Fawcett, MD, Beaumont (Allergy, Asthma and Immunology)
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